REMARKS

Claims 1-30 have been cancelled without prejudice. Applicants thank the Examiner for noting and renumbering the most recently added claims as claims 31-42. Claims 31-42 are pending.

Applicants also thank the Examiner for granting an interview with Applicants' representative on August 15, 2003. At the interview, patentability of the pending claims was discussed.

Claims 1-15 have been canceled. Thus, the rejections of these claims are moot.

Claims 31-42 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over the teachings of U.S. Patent No. 5,385,887 to Yim *et al.* ("Yim"), U.S. Patent No. 5,356,629 to Sander *et al.* ("Sander") and U.S. Patent No. 4,619,655 to Hanker *et al.* ("Hanker").

Claim 31, which is the only independent claim, features a bone graft substitute composition consisting of calcium sulfate hemihydrate, a mixing solution, and a plasticizing substance.

The transitional phrase "consisting of" excludes any element, step, or ingredient not specified in the claim. See MPEP 2111.03, citing In re Gray, 11 USPQ 255 (CCPA 1931); and Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948). Plasticizing substances include, for example, sodium carboxymethylcellulose, methylcellulose, hydroxypropyl methylcellulose, hydroxypropyl cellulose, ethylcellulose, hydroxyethylcellulose, and cellulose acetate butyrate.

The three ingredients required by claim 31 have been used previously in bone repair compositions, but never as the only three ingredients of the composition. The Examiner's position, basically, is that because the ingredients have been used previously in bone repair composition, it would have been obvious to use them, without other ingredients, in one composition.

Yim, Sander, and Hanker, taken alone or in combination, do not suggest a composition including only calcium sulfate, a mixing solution, and a plasticizing substance. Specifically, Hanker describes a bone repair composition that includes calcium sulfate, calcium phosphate particles, and water. The calcium phosphate particles are included to provide a source of

calcium over an extended period of time. (See, e.g., col. 3, lines 8-10.) The composition also can include other ingredients, such as medicaments, bone, and alumina. **Hanker's composition does not include a plasticizing substance such as a cellulose derivative.**

Yim describes compositions used to deliver osteogenic proteins to induce bone formation. The compositions include the osteogenic protein, a "porous particulate polymer matrix", autogenous blood, and calcium sulfate. Yim also says the composition optionally may include an additional osteogenic protein sequestering agent such as carboxymethylcellulose. (See, e.g., col. 2, lines 16-31.) Thus, **Yim describes a composition including the three ingredients required by claim 31, but only in combination with an osteogenic protein, a porous polymer particulate matrix, and autogenous blood.** Yim, alone or in combination with the other references, does not suggest removing the osteogenic protein, polymer matrix, or autogenous blood from the composition. In fact, removing the protein would run contrary to the reason Yim includes carboxymethyl cellulose in the composition--to sequester the protein.

The Examiner contends that Yim suggests adding carboxymethylcellulose to the bone repair composition described by Hanker. Specifically, the Examiner argues (see August 13, 2003 office action at 9):

> One of ordinary skill in the art would have been motivated to improve the workability of the composition of Hanker by the addition of the plasticizing substance disclosed by ... Yim.

But the Examiner's contention is factually wrong because Yim uses carboxymethylcellulose as a protein sequestering agent, not as a plasticizing substance. Hanker does not teach that his composition needs a protein sequestering agent. Moreover, even if a person of ordinary skill in the art decided to add the carboxymethylcellulose from Yim to the composition disclosed by Hanker, the resulting composition would not be a composition covered by the claims. The compositions covered by the claims include only three ingredients – calcium sulfate, the mixing solution, and the plasticizer. The composition that would result after adding the carboxymethylcellulose from Yim to the composition disclosed by Hanker also would include calcium phosphate particles and, presumably, an osteogenic protein for the protein sequestering agent to sequester.

Sander describes a bone repair composition including biocompatible particles (for example, made of polyglycolic acid) and a matrix material which can be a cellulosic material. Sander teaches that his composition is an improvement on compositions including calcium sulfate, which Sander says has undesirable workability and bioresorption (col. 1 lines 30-38):

> For example, plaster of paris [calcium sulfate hemihydrate] will tend to lose its workability and set hard within five to ten minutes after mixing with water, making it difficult to mold over an extended period of time to properly fit within a bone defect. Additionally, plaster of paris can take over one month to be resorbed after implantation into a bone defect, which limits the rate at which bone-forming cells can take the place left by resorbed plaster of paris.

Sander actually cites Hanker (at col. 1, line 18), apparently as an example of an unacceptable calcium sulfate-based composition.

Therefore, instead of using calcium sulfate, Sander uses a matrix material, such as a cellulosic material or collagen, to provide the composition with the good workability, resorption, and hardness upon setting. Sander contrasts his composition with one containing calcium sulfate (col. 2, lines 14-27):

> The composition of the present invention, when wetted, will not set into a rock hard material like plaster of paris which, when wetted, begins to set and lose workability within five to ten minutes. Therefore, the composition of the present invention retains workability or moldability characteristics for an extended period of time after being wetted, resulting in improved overall handling characteristics and ability to be shaped upon implantation into a bone defect site. Furthermore, the matrix in the composition of the present invention can be resorbed fairly rapidly upon implantation into a bone defect site, e.g., within about ten to fourteen days after implantation, permitting faster ingrowth of osteogenic cells as bone tissue is regenerated.

A person of ordinary skill in the art would not be motivated to combine the calcium sulfate from the composition described by Hanker or Yim with the composition disclosed by Sander at least because Sander stresses the undesirability of calcium sulfate Moreover, even if a person of ordinary skill in the art decided to add calcium sulfate to the composition described by Sander, the resulting composition would not be covered by the claims. The compositions covered by the claims include only three ingredients – calcium sulfate, the mixing solution, and the plasticizer. The composition that would result after adding the calcium sulfate

from Hanker or Yim to the composition disclosed by Sander would also include other ingredients such as the biocompatible particles.

Furthermore, a person of ordinary skill in the art would not be motivated to combine the matrix material (for example, a cellulosic derivative) from Sander with the composition described by Hanker. If anything, given Sander's teaching of the undesirability of calcium sulfate, a person of ordinary skill in the art would use the cellulosic material in place of the calcium sulfate in Hanker's composition. In addition, even if the person decided to combine the cellulosic derivative with the composition disclosed by Hanker, the resulting composition would not be covered by the claims. The compositions covered by the claims include only three ingredients – calcium sulfate, the mixing solution, and the plasticizer. The composition that would result after adding the matrix material from Sander to the composition disclosed by Hanker also would include other ingredients such as biocompatible particles.

Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a) of claims 31-42 based on Yim, Sander, and Hanker.

Applicants ask that all claims be allowed.

Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

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